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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/362,286 07/27/99 NADKARNI A CPI-099

000959
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HM12/0605

EXAMINER

MURPHY, J

ART UNIT

PAPER NUMBER

1644

10

DATE MAILED:

06/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/362,286

Applicant(s)

NADKARNI ET AL.

Examiner

Joseph F Murphy

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1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-42 is/are pending in the application.
- 4a) Of the above claim(s) 15-42 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) _____.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☒ Other: Sequence Comparison A, B

DETAILED ACTION

Election/Restrictions

1(a). Applicant's election with traverse of Group I, claims 1-14 in Paper No. 7, 5/1/2000 is acknowledged. The traversal is on the grounds that: i) the subject matter of the various groups represent different embodiments of a single inventive concept; ii) there is no burden on the examiner to consider all claims. This is not found persuasive for the following reasons.

1(b) Response to argument i): Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, Group I is classified in class 530, subclass 350; Group II is classified in class 435, subclass 254.2; Group III is classified in class 435, subclass 7.2. The separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. Thus, the Restriction requirement is proper.

1(c). Response to argument ii): Applicant argues that no burden is placed on the examiner to consider all claims. As discussed in (b), the separate classification established for each Group demonstrates that each distinct Group requires a separate field of search, and a search of one Group would not reveal art on the other Groups, thus imposing a burden on the examiner.

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1(d) The requirement is still deemed proper and is therefore made FINAL. Claims 15-42 are withdrawn from further consideration by the examiner, 37 CFR 1.48(b).

2. Claims 1-14 are under consideration.

Specification

3. The disclosure is objected to because of the following informalities: Amino acid sequences are not identified by SEQ ID NO's, for example, at page 20, lines 21 and 22, and page 62, lines 40-41.

Appropriate correction is required.

Formal Matters

4. Square brackets have been used in claims 1 and 14. Square brackets are to be used to indicate matter deleted from the claim due to an amendment. 37 CFR 1.121(a)(2)(ii) states:

(ii) Claim cancellation or rewriting: A claim may be amended by directions to cancel the claim or by rewriting such claim with underlining below the matter added and brackets around the matter deleted. The rewriting of a claim in this form will be construed as directing the deletion of the previous version of that claim. If a previously rewritten claim is again rewritten, underlining and bracketing will be applied relative to the previous version of the claim, with the parenthetical expression "twice amended," "three times amended," etc., following the original claim number. The original claim number followed by that parenthetical expression must be used for the rewritten claim. No interlineations or deletions of any prior amendment may appear in the currently submitted version of the claim. A claim canceled by amendment (not deleted and rewritten) can be reinstated only by a subsequent amendment presenting the claim as a new claim with a new claim number.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5(a). Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 defines a G protein coupled receptor by a function alone, i.e. that upon interaction with a ligand to modulate a signal transduction pathway in a cell, a signal generated by said mutant receptor is greater than a signal generated upon interaction of said ligand with a wild type G protein-coupled receptor. However, in *University of California v. Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 the Court decided that a definition by function alone "does not suffice" to sufficiently describe a sequence "because it is only an indication of what the gene does, rather than what it is." Further, "it is only a definition of a useful result rather than a definition of what achieves that result...The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention".

Claim 1 sets forth a definition of a mutant mammalian G protein coupled receptor. However, in *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1206, 18 USPQ2d 1016 at 1022 it was held that "when an inventor is unable to envision the detailed constitution of a

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gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e. until after the gene has been isolated". While Applicant has set forth the desired functions of a mutant mammalian G protein coupled receptor, Applicant has not set forth within the claim the detailed constitution of the mutant mammalian G protein coupled receptor, and thus does not satisfy the written description requirement.

5(b). Claims 1-14 are rejected under 35 U.S.C 112, first paragraph, because the specification, while being enabling for a mutant IL8 receptor and a mutant galanin receptor, does not reasonably provide enablement for any other mutant mammalian G protein coupled receptor. There is not adequate guidance as to the nature of the mutant mammalian G protein coupled receptor which Applicants claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim.

Claim 1 is overly broad in the recitation of "mutant mammalian G protein coupled receptor", since no guidance as to what constitutes "mutant mammalian G protein coupled receptor" is provided within the claims. The broad scope of claim 1 can be read to encompass any isolated mutant mammalian G protein coupled receptor. There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a mutant mammalian G protein coupled receptor other than those exemplified in the specification. See *In re Wands*, 858

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F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 1-14 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 2-14 are rejected insofar as they depend on the recitation in claim 1 of "mutant mammalian G protein coupled receptor".

Claim Rejections - 35 USC § 112 second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6(a). Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6(b). Claim 1 recites the limitation "said domain". There is insufficient antecedent basis for this limitation in the claim.

6(c). The term "varies" in claim 1 is a relative term which renders the claim indefinite. The term "varies" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 2-14 are rejected insofar as they depend on recitation of the term "varies" in claim 1.

6(d). The term "near" in claim 1 is a relative term which renders the claim indefinite. The term "near" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Claims 2-14 are rejected insofar as they depend on the recitation of the term "varies" in claim 1.

6(e). Claims 2 and 5 recite the limitation "said cell". There is insufficient antecedent basis for this limitation in the claim. Claim 1 is drawn to a mutant G protein coupled receptor, not a cell. Claims 3-4 are rejected insofar as they depend on recitation of the term "said cell" in claim 2.

6(f). Claims 8 and 13 are indefinite in that they only describe the peptide of interest by an arbitrary protein name. There is nothing in the claims which distinctly claims the protein and variants thereof. For example, others in the field may isolate the same protein and give said protein an entirely different name. Applicant should particularly point out and distinctly claim the receptors by claiming structural characteristics associated with the protein (e.g. amino acid

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sequence, molecular weight, etc.). Claiming biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly claim what that protein is.

6(g). Regarding claim 1, the phrase "such that" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7(a). Claims 1, 5, 8, 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Navarro et al. (WO 92/18641).

Navarro et al. discloses a mammalian IL8 receptor (page 10, lines 5-14). This receptor comprises a LFGA motif near the carboxy terminal (Figure 1, drawing Sheet 2, third line; Sequence Comparison A), and a seventh transmembrane domain. Navarro et al. discloses that specific receptor analogs include full-length or partial receptor proteins including an amino acid sequence which differs only by conservative amino acid substitutions, for example, substitution of one amino acid for another of the same class, or by one or more non-conservative amino acid substitutions, deletions, or insertions (page 10, line 32 to page 11, line 7). Thus claims 1, 8 and 11 are anticipated.

The receptor disclosed by Navarro et al. is expressed in mammalian cells (page 18, line 21-page 19, line 7), thus anticipating claim 5. The receptor cloned by Navarro et al. is human, thus anticipating claim 11.

7(b). Claims 1-2, 4-5 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Bergsman et al (WO 96/18651).

Bergsman et al. discloses a human somatostatin receptor (page 3, line 23). The receptor comprises a PPLA motif proximal to the carboxy terminal (page 21, third line; Sequence Comparison B), and a seventh transmembrane domain. Bergsman et al. discloses that mutants of the receptor may be prepared by the deletion of a portion of the sequence encoding the protein, by insertion of a sequence, and/or by substitution of one or more nucleotides within the sequence. The receptor disclosed in Bergsman et al. is expressed in human host cell lines (page 16, line 5), and yeast expression vectors are also envisaged (page 8, line 11) thus claims 1-2, 4-5 and 11-12 are anticipated.

7(c). Claims 1, 5 and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hinuma et al. (EP 0711830A2).

Hinuma et al. discloses a human galanin receptor (page 4, line 58 to page 5, line 8). The receptor comprises an FLSE motif near the carboxy terminal (page 58, amino acids 305-309), and a seventh transmembrane domain. Hinuma et al. discloses that the galanin receptor protein can be modified by, e.g., addition, deletion, substitution with other amino acids, etc (page 15,

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lines 49-50). The receptor disclosed in Hinuma et al. is expressed in 293 cells (page 18, lines 49-56). Thus, claims 1, 5 and 11-13 are anticipated.

Conclusion

8. No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703-308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1644
June 1, 2000


PREMA MERTZ
PRIMARY EXAMINER

PR 02-MAY-1994; US-237937.
 PA (REPK) REPLIGEN CORP.
 PI (UYBO-) UNIV BOSTON.
 PI Greenfield EA, Larosa GJ, Navarro J, Thomas KM;
 PI Wilt DT;
 DR WPI: 95-336945/43.
 N-PSDB: Q99949.
 PT Monoclonal antibody against recombinant IL-8 receptor polypeptide -
 PT useful for treating inflammatory disorders, for detecting
 PT neutrophil(s) and for isolating IL-8 receptor from liq.mixt.
 PS Claim 2; Fig 1A-B; 74pp; English.
 CC Monoclonal antibodies were raised against recombinant interleukin-8
 CC (IL-8) receptor subtypes A and B from both human and rabbit sources
 CC (R80950-53 encoded by Q99949-52). The A subtype receptor (IL-8RA) is
 CC a high affinity receptor and the B subtype receptor (IL-8RB) is
 CC low affinity receptor. The monoclonal antibody (mAb) pref. binds to
 CC the IL-8 binding domain thus blocking its activation. The mAbs are
 CC useful for treating inflammatory disorders (see key words) and for
 CC detecting the presence of neutrophils in a biological sample. The
 CC mAbs are also useful in the isolation of IL-8 receptors from a mixture.
 SQ Sequence 355 AA;

Query Match 100.0%; Score 217; DB 1; Length 355;
 Best Local Similarity 100.0%; Pred. No. 4,67e-14;
 Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

DB 298 LGFLHSLCLNPIIYAFIGNFRNGFLKM 324
 QY 1 LGFLHSLCLNPIIYAFIGNFRNGFLKM 27

Seoul Commission A

RESULT 3
 ID R28272 standard; Protein: 355 AA.
 AC R28272;
 DT 04-APR-1993 (first entry)
 DE Sequence in a high affinity recombinant rabbit interleukin-8
 DE (IL-8) receptor polypeptide in F3R.
 KM IL-8 receptor polypeptide; G-protein-coupled receptor.
 OS Oryctolagus cuniculus.
 PN W09218641-A.
 PD 29-OCT-1992.
 PF 10-APR-1992; U02977.
 PR 10-APR-1991; US-685101.
 PR 09-JUL-1991; US-726606.
 PR 09-DEC-1991; US-803842.
 PA (REPK) REPLIGEN CORP.
 PI (UYBO-) UNIV BOSTON.
 PI Navarro J, Thomas KM, Wilt DP;
 DR WPI: 92-382123/46.
 N-PSDB: Q30011.
 PT Recombinant mammalian interleukin-8 receptor - used for screening
 PT Interleukin-8 binding antagonists, used to treat inflammation
 PT Claim 2; Fig 1; 71pp; English.
 CC Rabbit high affinity IL-8 receptor gene was isolated from rabbit
 CC peritoneal neutrophils and used as a source of poly(A)+ RNA, to
 CC produce a rabbit neutrophil cDNA library. 250,000 recombinant
 CC plaques were screened for those which hybridized to an antisense
 CC oligonucleotide (Q30015). This probe was designed based on the
 CC sequence derived from the second transmembrane domain of G-protein-
 CC coupled receptors. After tertiary screening, six plaques were
 CC isolated. The insert of one of these plaques, termed F3R was of 2.5
 CC kb in size. The insert was sequenced. The protein deduced from
 CC the F3R clone demonstrates that it belongs to the family of
 CC G-protein-coupled receptors. The deduced protein sequence
 CC indicates seven putative transmembrane segments.
 SQ Sequence 355 AA;

Query Match 100.0%; Score 217; DB 1; Length 355;
 Best Local Similarity 100.0%; Pred. No. 4,67e-14;
 Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

298 LGFLHSLCLNPIIYAFIGNFRNGFLKM 324

QY 1 LGFLHSLCLNPIIYAFIGNFRNGFLKM 27

RESULT 4
 ID R68811 standard; Protein: 350 AA.
 AC R68811;
 DT 18-JUL-1995 (first entry)
 DE Interleukin-8 receptor.
 DE Interleukin-8 receptor; IL-8 receptor; PF4AR;
 KM Platelet factor superfamily receptor; neutrophil; chemotactic;
 KM inflammation; inflammatory disease; arthritis; emphysema; cystic;
 OS fibrosis; colitis; bronchitis; meningitis; therapeutic.
 OS Homo sapiens.
 PN W09428931-A.
 PD 22-DEC-1994.
 PF 07-JUN-1994; U06380.
 PF 11-JUN-1993; US-076093.
 PA (GENE) GENENTECH INC.
 PI Chuntcharapai A, Hebert C, Kim KJ, Lee J;
 DR WPI: 95-036114/05.
 N-PSDB: Q80520.
 PT Treatment of inflammatory disorders - by administering an
 PT antibody capable of binding a platelet factor 4 superfamily
 PT receptor polypeptide
 PS Disclosure; Page 51-54; 83pp; English.
 CC A cDNA library constructed from human neutrophil mRNA in pRSB was
 CC transfected into COS-7 cells, and the cells were screened with 125I-
 CC IL-8. The DNA sequence of isolated cDNA clone pRSB.1181.1,
 CC encoding human IL-8 receptor, is given in Q80520 and the predicted
 CC amino acid sequence in R68811. The receptor is used to raise
 CC antibodies that neutralize the activity of PF4AR, e.g. IL-8 receptor.
 SQ Sequence 350 AA;

Query Match 94.5%; Score 205; DB 1; Length 350;
 Best Local Similarity 92.6%; Pred. No. 9,05e-13;
 Matches 25; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

DB 293 LGFLHSLCLNPIIYAFIGNFRNGFLKI 319
 QY 1 LGFLHSLCLNPIIYAFIGNFRNGFLKM 27

RESULT 5
 ID R80756 standard; Protein: 350 AA.
 AC R80756;
 DT 26-MAR-1996 (first entry)
 DE Interleukin 8 receptor A partial sequence.
 KM Interleukin; IL-8; inflammation; psoriasis; dermatitis;
 KM rheumatoid arthritis; inflammatory bowel disease;
 KM chronic lung inflammation; treatment; antibody;
 OS affinity purification; detection.
 OS Homo sapiens.
 PN US5440021-A.
 PD 08-AUG-1995.
 PF 29-MAR-1991; 677211.
 PF 29-MAR-1991; US-677211.
 PR 25-FEB-1994; US-202056.
 PA (CHUN/) CHUNTHARAPAI A.
 PA (HEBE/) HERBERT C.
 PA (KIMK/) KIM K J.
 PA (LEEJ/) LEE J.
 PI Chuntcharapai A, Hebert C, Kim KJ, Lee J;
 DR WPI: 95-283151/37.
 N-PSDB: Q99006.
 PT New antibodies against interleukin 8 type B receptor - used to treat
 PT or prevent inflammation, also for detecting receptor expression and
 PT purification.
 PS Example 2; Columns 41-44; 62pp; English.
 CC Antibodies directed against the interleukin-8 receptor B can be used
 CC to treat or prevent inflammation e.g. psoriasis, dermatitis,
 CC rheumatoid arthritis and particularly inflammatory bowel disease and
 CC chronic lung inflammation. When immobilized, these antibodies may
 CC be used to detect interleukin-8 receptor B expression in cells and

